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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,186	11/16/2001	Martin Quibell	1718-0195P	8544

2292 7590 09/03/2003

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EXAMINER
MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/03/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,186	QUIBELL ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12,16-38 and 41* is/are allowed.

6)☒ Claim(s) *1,2,5-10,13-15,39 and 40* is/are rejected.

7)☒ Claim(s) *3,4 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to an application filed on 11/16/01. There are forty-one claims pending and forty-one under consideration. Claims 1-12 and 16-36 are compound claims. Claims 13, 37, and 38 are composition claims. Claims 14, 15, and 39 are use claims. Claims 40 and 41 are method of synthesis claims. This is the first action on the merits. The application concerns some 2-Pentulose and 5-Oxo-2H-Pyran compounds, compositions, and uses thereof.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5-10, and 13-15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In line 8 of claim 1, because of the punctuation, Applicants are claiming that X can be Z, which in turn, can be CH. This is not what is intended. The Examiner suggests deleting the comma after the variable X and replacing the comma after "NH" with a semicolon.

3. Claims 14, 15, and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not set forth any steps involved in determining how to identify which patients need

"inhibiting the cysteine protease Cathepsin S". It is unclear what diseases and treatments applicant is intending to encompass. Determining whether a given disease responds or does not respond to such an enzyme inhibitor and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases Applicants intend to treat, the physician skilled in the clinical arts cannot determine the metes and bounds of the claim. Hence, the claims are indefinite.

Nowhere does the specification describe any process for identifying which patients are in need of such treatment. The passage spanning pages 9 to 10 lists a number of conditions but uses open language to do so, "examples", "and the like". What other patients are included? Oballa ('036) states that Alzheimer's disease, juvenile onset diabetes, pemphigus vulgaris, Graves' disease, myasthenia gravis, and systemic lupus erythemotasus are such diseases. None of these are included in Applicants list. Are these diseases to be included or not?

4. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 40, the phrase "for example" renders the claim indefinite because it is unclear whether the

limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 15, and 39 rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating any human disease. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement requirement, when applied to process claims refers to carrying out the claimed process.

The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Determining if any particular claimed compound would treat any particular Cathepsin S related disease would require synthesis of the

compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different Cathepsin S related diseases discussed above, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large degree of experimentation. b) The direction concerning treating Cathepsin S related diseases is found in the passage spanning pages 9 and 10, which merely states Applicants' intention to do so. Applicants describe formulations in paragraph 4, page 13. There are no working examples of any formulation. Doses required to practice their invention are described in paragraph 2, page 15. A 10,000-fold range of doses is recommended. Since no Cathepsin S inhibitor has ever been used to treat any human disease, how is the skilled physician to know what dose to use for each of these different diseases? There is an *in vitro* assay described in the passage spanning page 124 to the third paragraph on page 125 but it is unclear if this assay is correlated to human diseases. c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease, which involves physiological activity. e) The state of the clinical arts in Cathepsin S related diseases is provided by Katunuma (FEBS Letters) who states that in 1999 no inhibitors of this enzyme were known. Logically no clinical uses of such inhibitors could have beeen known in 1999. Villadangos (Immunol. Rev.) states

that therapeutical applications of such inhibitors were possible but by implication unknown at that time.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The scope of the claims involves all of the thousands of compounds of claim 1 as well as the hundred of diseases embraced by the term Cathepsin S related. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

6. Claims 14, 15, and 39 rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating any human

disease. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. The how to use portion of the statute means that Applicants must teach the skilled practitioner, in this case a physician, what diseases and what symptoms she is to treat. The rejected claims are drawn to treatment of patients who need "inhibiting the cysteine protease Cathepsin S", which as recited reads on the treatment of any and all diseases for which there is no enabling disclosure. This scope of disease treatment is not adequately supported based solely on the testing data provided in the specification at pages 124-125. The specification at pages 9 and 10 asserts that the compounds are useful for treating all sorts of diseases for which Applicants have provided no empirical support. The recent reviews of Cathepsin S discussed above states that use of such inhibitors is still in the experimental stage and is speculative in nature. Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual", or not provided in the specification, *Ex parte Jovanovics,* 211 USPQ 907, *In re Langer,* 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 200 USPQ 925 concerning the type of testing needed to support *in vivo* use claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 14, 15, and 39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. The references discussed above establish that in 1999 no disease was known to be treatable by inhibitors of Cathepsin S. Additionally, Saegusa (J. Clin. Invest.) shos tht even by 2002 no clinical uses of such inhibitors were recognized.

Allowable Subject Matter

8. Claims 12, 16-38, and 41 are allowed. Claims 3, 4, and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 1, 2, 5-10, and 13 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Conclusion

9. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for amendments is (703)

872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK